Access DB# 34820

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: SHARON FOLEY Examiner #: 72857 Date: 2/5/01
Art Unit: 1648 Phone Number 308-3983 Serial Number: 09/617569
Mail Box and Bldg/Room Location: 8C12/8819 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Heteroduplex complexes and methods

Inventors (please provide full names): Petrus ROELVINK; Joseph GRUBER; Jane KOVESDI; Thomas J. WICKHAM

Earliest Priority Filing Date: 7/9/00

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please include an inventor name search.

Please search for a complex comprising a virion (empty or sulkes) that has viral capsid proteins within it. The complex has a non-native ligand that recognizes an epitope on an immune effector cell (MHC I +/or II) and a nucleic acid that encodes a non-native antigen. CD-40 and has an RGD motif or fragment

(G4,610,636,580,595 G5,275,364 G5,511,580,595 G4,610,636,580,603 G5,275,370 G5,511,580,600)

The ligand recognizes lysine +/or histidine residues.

The complex also has a liposome, lipid bilayers ligand D26,600,480 radioligand assay receptor(s) cell surface

The virus is non-enveloped + has an adenovirus capsid.

- Also this is in a pharmaceutical composition.

Virion B4,950

epitope D24,611,216,550 antibody? (a) anti idiotyp? antibody affinity epitope mapping molecular markers antigen? (a) (determine? specify?) Thank you.

Capsid B4,950,500,250 D12,776,964,980,800 250 Virus particle capsid protein coat protein viral coat protein

Please give to Mary Hale. Claims 1-32 + 40-43 only.

****

STAFF USE ONLY

Searcher: [illegible]
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed: 2/9
Searcher Prep & Review Time: 14
Clerical Prep Time:
Online Time: 9

Type of Search

NA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN 125, 24
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (1-2000)

Foley
617569

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=> fil medl,caplus,biosis,embase,wpids,jicst

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'MEDLINE' ENTERED AT 10:10:03 ON 09 FEB 2001

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FILE 'JICST-EPLUS' ENTERED AT 10:10:03 ON 09 FEB 2001
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=> s (virion or b4.950/ct or virus particle) and (capsid or b4.950.500.250/ct
or d12.776.964.970.600.250/ct or capsid protein or coat? protein or viral
coat? protein)

L1          2813 FILE MEDLINE
L2          3096 FILE CAPLUS
L3          2645 FILE BIOSIS
L4          2343 FILE EMBASE
L5            77 FILE WPIDS
L6           130 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L7         11104 (VIRION OR B4.950/CT OR VIRUS PARTICLE) AND (CAPSID OR
B4.950.50
                 0.250/CT OR D12.776.964.970.600.250/CT OR CAPSID PROTEIN OR
                 COAT? PROTEIN OR VIRAL COAT? PROTEIN)

=> s l7 and (liposome or lipid bilayer! or ligand or d26.600.480/ct or
radioligand assay or receptor!(a)cell surface)

L8            52 FILE MEDLINE
L9            64 FILE CAPLUS
L10           31 FILE BIOSIS
L11           43 FILE EMBASE
L12            3 FILE WPIDS
L13            1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L14          194 L7 AND (LIPOSOME OR LIPID BILAYER! OR LIGAND OR D26.600.480/CT
                 OR RADIOLIGAND ASSAY OR RECEPTOR!(A) CELL SURFACE)
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=> s l14 and (epitope or d24.611.216.550/ct or antibod?(a)anti idiotyp? or
antibod? affinity? or epitope map? or molecular mimicry or
antigen(w)(determin? or specif?))

L15           7 FILE MEDLINE
L16          11 FILE CAPLUS
L17           4 FILE BIOSIS
L18           5 FILE EMBASE
L19           0 FILE WPIDS
L20           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L21          27 L14 AND (EPITOPE OR D24.611.216.550/CT OR ANTIBOD?(A) ANTI
IDIOT
                YP? OR ANTIBOD? AFFINITY? OR EPITOPE MAP? OR MOLECULAR MIMICRY
                OR ANTIGEN(W)(DETERMIN? OR SPECIF?))

=> s l21 and (mhc(w)(i or ii) or (g4.610.626.580.595 or g5.511.580.595 or
g5.275.364 or g4.610.626.580.600 or g5.275.370 or g5.511.580.600)/ct)

L22           0 FILE MEDLINE
L23           0 FILE CAPLUS
L24           0 FILE BIOSIS
L25           0 FILE EMBASE
L26           0 FILE WPIDS
L27           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L28           0 L21 AND (MHC(W)(I OR II) OR (G4.610.626.580.595 OR
G5.511.580.59
                5 OR G5.275.364 OR G4.610.626.580.600 OR G5.275.370 OR
G5.511.58
                0.600)/CT)

=> s l21 and cd40

L29           0 FILE MEDLINE
L30           1 FILE CAPLUS
L31           0 FILE BIOSIS
L32           0 FILE EMBASE
L33           0 FILE WPIDS
L34           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L35           1 L21 AND CD40

=> s l21 and rgd motif

L36           0 FILE MEDLINE
L37           0 FILE CAPLUS
L38           0 FILE BIOSIS
L39           0 FILE EMBASE
L40           0 FILE WPIDS
L41           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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L42 0 L21 AND RGD MOTIF

=> s rgd and l21

L43 1 FILE MEDLINE
L44 1 FILE CAPLUS
L45 1 FILE BIOSIS
L46 1 FILE EMBASE
L47 0 FILE WPIDS
L48 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L49 4 RGD AND L21

=> d l35 cbib abs;s 149 not 135

L35 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
1996:676262 Document No. 125:319219 Immunology of gene therapy with adenoviral vectors in mouse skeletal muscle. Yang, Yiping; Haecker, Sarah Ehlen; Su, Qin; Wilson, James M. (Inst. for Human Gene Therapy, Univ. Pennsylvania Medical Center and Wistar Inst., Philadelphia, PA, 19104, USA). Hum. Mol. Genet., 5(11), 1703-1712 (English) 1996. CODEN: HMGEE5. ISSN: 0964-6906.

AB Skeletal muscle is an attractive target for somatic gene transfer of both acquired and inherited disorders. Direct injection of adenoviral vectors in the skeletal muscle leads to recombinant gene expression in a large no. of muscle fibers. Transgene expression has been transient in most organs and assocd. with substantial inflammation when expts. are performed in adult immune competent mice. In this report, we utilize a variety of in vivo and in vitro models of T and B cell function to characterize the nature of the immune response to adenoviral vectors injected into murine skeletal muscle. Cellular immunity dependent on CD4+ and CD8+ T cells contributes to the loss of recombinant gene expression and the development of localized inflammation. **Antigen specific** activation of T cells occurs to both viral proteins and the reporter gene .beta.-galactosidase. Systemic levels of neutralizing antibody to the **capsid proteins** of the vector are also generated. Destructive immune responses responsible for loss of transgene expression are largely directed against .beta.-galactosidase in that transgene expression was stable when .beta.-galactosidase was eliminated as a neoantigen in mice transgenic for lacZ. A strategy to prevent the cellular and humoral immunity to this therapy was developed based on transiently ablating CD4+ T cell activation at the time of vector delivery. Encouraging results were obtained when vector was administered with one of several immune modulating agents including cyclophosphamide, mAb to CD4+ cells, and mAb to **CD40 ligand**. These studies indicate that cellular and humoral immune responses are elicited in the context of gene therapy directed to skeletal muscle with adenoviral vectors. Transient ablation of CD4+ T cell activation prevents the effector responses of the CD8+ T and B cells.

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L50             1 FILE MEDLINE
L51             1 FILE CAPLUS
L52             1 FILE BIOSIS
L53             1 FILE EMBASE
L54             0 FILE WPIDS
L55             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L56             4 L49 NOT L35

=> dup rem l56

PROCESSING COMPLETED FOR L56
L57             1 DUP REM L56 (3 DUPLICATES REMOVED)

=> d cbib abs


L57  ANSWER 1 OF 1  MEDLINE                                  DUPLICATE 1
1998443237  Document Number: 98443237.   Conformational flexibility in a
highly
     mobile protein loop of foot-and-mouth disease virus: distinct structural
     requirements for integrin and antibody binding. Feliu J X; Benito A;
Oliva
     B; Aviles F X; Villaverde A. (Institut de Biologia Fonamental,
Universitat
     Aut`onoma de Barcelona Bellaterra, 08193 Barcelona Spain. ) JOURNAL OF
     MOLECULAR BIOLOGY, (1998 Oct 23) 283 (2) 331-8.  Journal code: J6V. ISSN:
     0022-2836. Pub. country: ENGLAND: United Kingdom. Language: English.
AB   The G-H loop of foot-and-mouth disease virus VP1 protein is a highly
     mobile peptide, that extends from the capsid surface and that in
     native virions is invisible by X-ray crystallography. In
     serotype C, this segment contains a hypervariable region with several
     continuous, overlapping, B-cell epitopes that embrace the
     conserved Arg-Gly-Asp (RGD) cell attachment motif. The
     solvent-exposed positioning of this peptide by selective insertion into
     different structural frameworks of E. coli beta-galactosidase, generates
a
     spectrum of antigenic variants which react distinctively with a panel of
     anti-VP1 monoclonal antibodies and exhibit different efficiencies as cell
     ligands. The cell attachment efficiency is much less restricted by
     the different positioning of the viral segment at the insertion sites. A
     molecular model of an inserted stretch reveals a highest flexibility of
     the RGD tripeptide segment compared with the flanking sequences,
     that could allow a proper accommodation to integrin receptors even in
     poorly antigenic conformations. The non-converging structural
requirements
     for RGD-mediated integrin binding and antibody recognition,
     explains the dynamism of the generation of neutralisation-resistant
     antigenic variants in the viral quasi-species, arising from a
     conformational space of integrin-binding competent peptides. This might
be
     of special relevance for foot-and-moth disease virus evolution, since
     unlike in other picornaviruses, the cell binding motif and the major
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neutralising B-cell **epitopes** overlap in a solvent-exposed peptide accessible to the host immune system, in a **virion** lacking canyons and similar hiding structures. Copyright 1998 Academic Press.

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=> s roelvink p?/au,in;s bruder j?/au,in;s kovesdi i?/au,in;s wickham t?/au,in

'IN' IS NOT A VALID FIELD CODE
L58          16 FILE MEDLINE
L59          29 FILE CAPLUS
L60          28 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L61          15 FILE EMBASE
L62           7 FILE WPIDS
L63           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L64          95 ROELVINK P?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L65          47 FILE MEDLINE
L66          56 FILE CAPLUS
L67          62 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L68          46 FILE EMBASE
L69          25 FILE WPIDS
L70           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L71         236 BRUDER J?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L72          93 FILE MEDLINE
L73         140 FILE CAPLUS
L74         124 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L75          88 FILE EMBASE
L76          24 FILE WPIDS
L77           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L78         469 KOVESDI I?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L79          41 FILE MEDLINE
L80          56 FILE CAPLUS
L81          57 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L82          37 FILE EMBASE
L83          16 FILE WPIDS
L84           0 FILE JICST-EPLUS
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TOTAL FOR ALL FILES
L85 207 WICKHAM T?/AU,IN

=> s l64 and l71 and l78 and l85

L86 0 FILE MEDLINE
L87 3 FILE CAPLUS
L88 0 FILE BIOSIS
L89 0 FILE EMBASE
L90 3 FILE WPIDS
L91 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L92 6 L64 AND L71 AND L78 AND L85

=> dup rem l92

PROCESSING COMPLETED FOR L92
L93 3 DUP REM L92 (3 DUPLICATES REMOVED)

=> d cbib abs 1-3

L93 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2000:191242 Document No. 132:232728 Adenovirus having a modified fiber protein leading to reduced targeting for the native adenoviral receptor. **Wickham, Thomas J.**; Kovesdi, Imre; Roelvink, Petrus W.; Bruder, Joseph T. (Genvec, Inc., USA). PCT Int. Appl. WO 2000015823 A1 20000323, 69 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US20728 19990910. PRIORITY: US 1998-99851 19980911; US 1999-136529 19990528.

AB The present invention provides an adenovirus comprising a recombinant fiber protein having modifications in the N-terminal, trimerization knob domain. A fiber incorporating such a protein exhibits reduced affinity for the native CAR protein substrate (coxsackievirus and adenovirus receptor) than does a wild-type adenoviral fiber trimer. Site-specific mutagenesis and competition expts. identified residues in the AB loop, B sheet, DE loop, and FG loop as important for CAR binding and conserved among adenoviral serotypes. An adenovirus serotype 5 mutant contg. a deletion in the FG loop (.DELTA.T489AYT492) was further modified by introducing the hemagglutinin (HA) epitope into the HI loop of the fiber knob (between amino acids 543 and 544). The result adenoviruses exhibit reduced binding capacity to CAR on std. HEK-293 cells due to the TAYT deletion; however, it binds with high affinity via its HA epitope to an anti-HA pseudoreceptor present on an anti-HA-293 cell line. Addnl. modifications may include the introduction of a high affinity RGD ligand. The present invention permits more efficient prodn. and construction of safer adenoviral vectors for gene transfer applications.

L93 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
1998:75999 Document No. 128:150383 Adenoviral-mediated cell targeting commanded by the adenovirus penton base protein. **Wickham, Thomas J.**; Kovesdi, Imre; Roelvink, Petrus W.; Brough, Douglas E.; McVey, Duncan L.; Bruder, Joseph T. (Genvec, Inc., USA). U.S. US 5712136 A 19980127, 56 pp. Cont.-in-part of U.S. 5,559,099. (English). CODEN: USXXAM. APPLICATION: US 1996-634060 19960417. PRIORITY: US 1994-303162 19940908.

AB A method of introducing an adenovirus into a cell comprises a particular cell surface binding site as well as a chimeric adenovirus penton base protein, and recombinant adenoviral vectors comprising the chimeric adenovirus penton base protein for use in the method are provided. The adenovirus is contacted with a bispecific mol. (antibody) comprising (1) a component that selectively binds to a domain of the penton base protein of the adenovirus, and (2) a second component that selectively binds the particular cell surface site. Binding of the fiber protein of the adenovirus to any cell surface mol. is abrogated (e.g., by the introduction of a protease cleavage site), and the cell binds to a specific site introduced into the penton base protein of the adenovirus. The construction of chimeric adenovirus penton base protein and recombinant adenoviral vectors is described.

L93 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
1996:621434 Document No. 125:238646 Adenovirus gene therapy vectors using fiber protein fusion proteins for efficient targetting of the virus. **Wickham, Thomas J.**; Falck-Pedersen, Erik; Roelvink, Petrus W.; Bruder, Joseph T.; Gall, Jason; Kovesdi, Imre (Genvec, Inc., USA; Cornell Research Foundation, Inc.). PCT Int. Appl. WO 9626281 A1 19960829, 61 pp.
DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US1957 19960213. PRIORITY: US 1995-395381 19950221.

AB Adenovirus gene therapy vectors that have the receptor-binding domain of the viral fiber protein substituted by a protein ligand for a specific receptor and that carry a therapeutic gene are described. A series of constructs in which the receptor binding domain of the adenovirus 5 fiber protein is replaced with the corresponding domain of other adenovirus fiber proteins or integrins is described. Use of the sialic acid-binding domain of the adenovirus 3 fiber protein gives rise to a virus that will bind to all known eukaryotic cell types. In vivo tests using a reporter gene construct showed that partial substitution of the Ad5 fiber protein with the Ad7 fiber protein did not affect infectivity of the virus.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	125.09	125.24

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.35	-2.35

STN INTERNATIONAL LOGOFF AT 10:19:45 ON 09 FEB 2001

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:36:35 ON 19 FEB 2001

L1	1204358	S	VIRUS OR VIRION
L2	9	S	NON-NATIVE LIGAND?
L3	0	S	L1 AND L2
L4	264690	S	LIGAND?
L5	1918	S	HETEROLOGOUS AND L4
L6	138	S	L5 AND L1
L7	1	S	CD40 AND L6
L8	8752	S	CD40
L9	4197	S	L8 AND L4
L10	16	S	L8 AND L5
L11	1	S	L10 AND L1
L12	1188	S	IMMUNE EFFECTOR CELL?
L13	0	S	L12 AND L6
L14	0	S	L12 AND L5
L15	1200364	S	ANTIGEN?
L16	15434	S	HETEROLOGOUS AND L15
L17	3431	S	L16 AND L1
L18	58232	S	ADENOVIR?
L19	118	S	L17 AND 18
L20	7	S	L5 AND RGD
L21	3		DUP REM L20 (4 DUPLICATES REMOVED)
L22	61995	S	LIPOSOME
L23	4419	S	L1 AND L22
L24	0	S	L23 AND L5
L25	110	S	L23 AND L4
L26	24	S	L25 AND L15
L27	16		DUP REM L26 (8 DUPLICATES REMOVED)
L28	158	S	ADENOVIR? CAPSID
L29	127	S	L28 AND L1
L30	0	S	NUCLEIC ACID VIRAL GENOME
L31	14655	S	VIRAL GENOME
L32	202794	S	NUCLEIC ACID?
L33	1672	S	L31 AND L32
L34	0	S	L33 AND L29
		E	ROELVINK/AU
		E	ROELVINK PETRUS/AU
		E	ROELVINK PETRUS OR P/AU
L35	0	S	E4 AND LL5
		E	T WICKHAM/AU
		E	WICKHAM THOMAS/AU
L36	81	S	E2 OR E3 AND L5
L37	8	S	L36 AND L15
L38	6		DUP REM L37 (2 DUPLICATES REMOVED)
L39	0	S	L36 AND L8
L40	0	S	L39 AND L12
L41	0	S	L36 AND L12
L42	24	S	L26 AND L22
L43	16		DUP REM L42 (8 DUPLICATES REMOVED)